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#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Timothy A. Coleman

Docket No.: PF112P6

Application No.: 09/921,143

Group Art Unit: 1653

Filed: August 3, 2001

Examiner: Not Yet Assigned

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For: Vascular Endothelial Growth Factor 2

#### SUBMISSION OF REPLACEMENT/SUBSTITUTE DRAWINGS

Attn: Draftsperson Commissioner for Patents Washington, DC 20231

Sir:

Applicants submit herewith replacement/substitute Figures 1A-31U (68 sheets) to replace Figures 1A-31G (47 sheets) as originally filed. Additional pages are due to reorganization of the drawings in order to comply with the margin requirements under 37 C.F.R. § 1.84. No new matter is introduced.

No fee is believed due for this submission. In the event that a fee is required in connection with this submission, please charge the required fee to Deposit Account No. 08-3425.

Respectfully submitted,

Dated: April 17, 2003

Melissa J. Pytel

Registration No. 41,512

HUMAN GENOME SCIENCES, INC.

9410 Key West Avenue Rockville, Maryland 20850

(301) 610-5764

Attorney for Applicants



360	CCAACCTCAACTCAAGGACAGAAGAGACTATAAAATTTGCTGCAGCACATTATAATACAG +++++++	301
300	ATTGGAAAATGTACAAGTGTCAGCTAAGGAAGGAGGCTGGCAACATAACAGAGAACAGG ++++++	241
240	AGGAGCAGTTACGGTCTGTGTCCAGTGTAGATGAACTCATGACTGTACTCTACCCAGAAT+++++ TCCTCGTCAATGCCAGACACAGGTCACATCTACTTGAGTACTGACATGAGATGGGTCTTA EQLRSVDBELMITVLYL	181
180	ACCTCTCGGACGCGCGCGGGCGAGGCCACGGCTTATGCAAGCAA	121
120	GCGACGAGGCCCCAGGAGCGCTCCGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCG	61
09	CAGGAAGGTGGTACGTGAGCGACCCGAAGAGAGACACCGCACAAGAGACGACGGCGAC M H S L G F F S V A C S L L A A A	ı
,	GTCCTTCCACCATGCACTCGCTGGGCTTCTTCTCTGTGGCGTGTTCTCTGTGCCTCGCCGC	Н

FIG. 1A

MATCH WITH FIG. 1B

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## MATCH WITH FIG. 1A

TCTAGAACTTTTCATAACTATTACTCACCTCTTTCTGAGTTACGTACG

FIG. 18

MATCH WITH FIG. 1C



## MATCH WITH FIG. 1B

, ,	GCCCCGAAGCCGGACGGTCGACACCTGGGGTGTTTCTTGATCTGTCTTTGAGTACGGTCA G L R P A S C G P H K E L D R N S C O C	 
0	CGGGGCTTCGGCCTGCCAGCTGTGGACCCCCACAAGAACTAGACAGAAACTCATGCCAGT	901
70	TACTGTAGACACCTGGTTTGTTCCTCGACCTACTTCTCTGGACAGTCACACAGACGTCTC DICGPNTTGTTCTTCGACCTACTTCTCTGGACAGTCACAGACGTCTC	₹ 0
000	ATGACATCTGTGGACCAAACAAGGAGCTGGATGAAGAGACCTGTCAGTGTGTGT	841
84(	ACCGAGTCCTTCTAAAATACAAAAGGAGCCTACGACCTCTACTGAGTTGTCTACCTAAGGAGCCTACGACCTCTACTGAGTTGTCTACCTAAGGAGCCTACGACCTCTACTGAGTTGTCTACCTAAGGAGCCTACGACCTCTACTGAGTTGTCTACCTAAGGAGCCTACGACCTCTACTGAGTTGTCTACCTAAGGAGCCTACGACCTCTACTGAGTTGTCTACCTAAGGAGCCTACGACCTCTACTGAGTTGTCTACCTAAGGAGCCTACGACCTCTACTACAAAGGAGCCTACGACCTCTACAAAGGAGCCTACGACTACAAAAGGAGCCTACGACTACAAAAGGAGCCTACGACTACAAAAGGAGCCTACGACAAAAAAAA	T8/
0	TGGCTCAGGAAGATTTTATGTTTTTCCTCGGATGCTGGAGATGACTCAACAGATGGATTCC	781
	TCCGTCGCTTGTTCTGGACGGGGGGGTGGTTAATGTACACCTTATTAGTGGACGTCTACGG	<b>!</b>
787	AGGCAGCGAACAAGACCTGCCCCACCAATTACATGTGGAATAATCACATCTGCAGATGCC	721
	AAATGTCTGTTCAAGTAAGGTAATAATCTGCAAGGGACGGTCGTTGTGATGGTGTCACAG	i ) )
700	TTTACAGACAAGTTCATTCCATTATTAGACGTTCCCTGCCAGCAACACTACCACAGTGTC	661

FIG. 10

MATCH WITH FIG. 1D



## MATCH WITH FIG. 1C

1020	1080	1140	1200	1260
GTGTCTGTAAAACAAACTCTTCCCCAGCCAATGTGGGGCCAACCGAGAATTTGATGAAA ++++++	ACACATGCCAGTGTGTATGTAAAGAACCTGCCCCAGAAATCAACCCCTAAATCCTGGAA ++++++	AATGTGCCTGTGAATGTACAGAAAGTCCACAGAAATGCTTGTTAAAAGGAAAGAAGTTCC++++++++ TTACACGGACACTTACATGTCTTTCAGGTGTCTTTACGAACAATTTTCCTTTCTTCAAGG	ACCACCAAACATGCAGCTGTTACAGACGGCCATGTACGAACCGCCAGAAGGCTTGTGAGC++++++ TGGTGGTTTGTACGTCGACAATGTCTGCCGGTACATGCTTGGCGGTCTTCCGAACACTCG H Q T C S C Y R R P C T N R Q K A C E P	CAGGATTTTCATATAGTGAAGAGTGTGTCGTTGTGTCCCTTCATATTGGCAAAGACCAC++++ GTCCTAAAAGTATATCACTTCTTCACACAGCAACACAGGGAAGTATAACCGTTTCTGGTG G F S Y S E E V C R C V P S Y W Q R P Q
961	1021	1081	1141	1201

FIG. 1D

MATCH WITH FIG. 1E



## MATCH WITH FIG. 1D

;	AGCTAAGATTGTACTGT	1200
1261	TTTACTCGATTCTAACATGACAAAAGGTCAAGTAGCTAAAAGATAATACCTTTTGACACA M S *	0 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7
1321	TGCCACAGTAGAACTGTCTGTGAACAGAGACCCTTGTGGGTCCATGCTAACAAAGACA	1380
1761	ACGGTGTCATCTTGACAGACACTTGTCTCTCTGGGAACACCCCAGGTACGATTGTTTCTGT	
,	AAAGTCTGTCTTTCCTGAACCATGTGGATAACTTTACAGAAATGGACTGGAGCTCATCTG	1770
1381	TTTCAGACAGAAAGGACTTGGTACACCTATTGAAATGTCTTTACCTGACCTCGAGTAGAC	) F H
, ,	CAAAAGGCCTCTTGTAAAGACTGGTTTTCTGCCAATGACCAAACAGCCAAGATTTTCCTC	1500
T # # T	GTTTTCCGGAGAACATTTCTGACCAAAAGACGGTTACTGGTTTGTCGGTTCTAAAAGGAG	) ) 
, ,	TTGTGATTTCTTTAAAAGAATGACTATATAATTTTATTTCCACTAAAAATATTGTTTTCTGC	1 0 0 0
TOCT	AACACTAAAGAAATTTTCTTACTGATATATTAAATAAGGTGATTTTTTATAACAAAGACG	) ) )
	ATTCATTTTTATAGCAACAACAATTGGTAAAACTCACTGTGATCAATATTTTTATATCAT	1620
1561	TAAGTAAAAATATCGTTGTTGATTAACCATTTTGAGTGACACTAGTTATAAAAATATAGTA	H N
7		1674
1621	+++	ተ ጋ

FIG. 1E

#### 2A

# MATCH WITH FIG. 2B

CGCGACAAACACCTTCTTTAAACCTCCATGTGTGTCCGTCTACAGATGTGGGGGTTGCTG	101
EVCIDVGKEFG	
GAGAAAGACTCAATGCATGCACGGGAGGTGTGTATAGATGTGGGGAAGGAGTTTGGAGT	41
IKFAAHYNTEILKSIDNEW	
TATAAAATTTGCTGCAGCACATTATAATACAGAGATCTTGAAAAGTATTGATAATGAGTG 	.81
K G G W Q H N R E Q A N L N S R T E E T	
GAAAGGAGGCTGGCAACATAACAGAGAACAGGCCAACCTCAACTCAAGGACAGAAGAGACACACAC	.21
M T V L Y P E Y W K M Y K C Q L R	
* AGATGAACTCATGACTGTACTCTACCCAGAATATTGGAAAATGTACAAGTGTCAGCTAAG	1.
+!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!	
CGAGGCCACGGCTTATGCAAGCAAAGATCTGGAGGAGCAGTTACGGTCTGTGTCCAGTGT	



# MATCH WITH FIG. 2A

421	* TGAAATTACAGTGCCTCTCTCTCAAGGCCCCCAAACCAGTAACAATCAGTTTTGCCAATCA
	P L S Q G P K P V T I S F A N
481	GATGCATGTCTAAACTGGATGTTTACAGACAAGTTCATTCCATTAT
	T S C R C M S K L D V Y R Q V H S I I R
541	CCCTGCCAGCAACACTACCACAGTGTCAGGCAGCGAACAAGACCTGCCCCAC
	RSLPATLPQCQAANKTCPTN
601	ATAATCACATCTGCAGATGCCTGGCTCAGGAAGATTTTATGTTTTCC
	Y M W N N H I C R C L A Q E D F M F S S
661	GGATGCTGGAGATGACTCAACATGCATGACATCTGTGGACCAAACAAGGAGCT
	DAGDDSTDGFH
721	GGATGAAGAGACCTGTCAGTGTGTCTGCAGAGCGGGGCTTCGGCCTGCCAGCTGTGGACC
	DEETCOCVCRAGLRPASCGP
	MATCH WITH FIG. 2C

FIG. 2B



## MATCH WITH FIG. 2B

ATGTGGGGCCAACCGAGAATTTGATGAAAACAC  C G A N R E F D E N T  CCCCAGAAATCAACCCCTAAATCCTGGAAAATG  CCCCAGAAATCAACCCCTAAATCCTGGAAAATG  CCCCAGAAATCAACCCCTAAATCCTGGAAAATG  ATGTACGAACCGCCAGAAGGAAGGAAGGACCAGG  ATGTACGAACCGCCAGAAGGCTTGTGAGCCAGG  C T N R Q K A C E P G  CT N R Q K A C E P G  CT N R Q K A C E P G  CT N R Q K A C E P G	CCACAAAGAACTAGACAGAAACTCATGCCAGTGTGTCTGTAAAAAACAAAC	GTCTGTAAAACAAACTCTTCCCCA(
CCAATGTGGGCCAACCGAGATTTGATGAAAACACATGCCAGTGTGTAAAAA  OCGAAN REFDENTCOTTGAAATGTGCCTGTGAATGTAAAA  CTGCCCCAGAAATCAACCCCTAAATCCTGGAAATGTGCCTGTGAATGTACAGAAA  CTGCCCCAGAAATCAACCCCTAAATCCTGGAAATGTGCCTGTGAATGTACAGAAA  CPRNQPLNPGCAAATGCTGTTAAAAGGAAAGAAATGTCCACCAAAATGTGCTTTACA  ACAGAAATGCTTGTTAAAAGGAAAGAAAGAAGACCACCAAAATGTGAAGAAGG  ORCATGTACGAACCGCCAGAAGGCTTGTGAGAGATTTTCATATAGTGAAGAAGG  GCCATGTACGAACCGCCAGAAGACTTGTGAGAATTTTCATATAGTGAAGAAGGAAG	K E L D R N S C Q C	++ C K N K L
CTGCCCCAGAAATCAACCCCTAAATCTGGAAAATGTGCCTGTGAATGTACAGAAA  C P R N Q P L N P G K C A C E C T E S  ACAGAAATGCTTGTTAAAAGGAAAGAAAGAAACACCCCACAACATGCAGCTGTTACA  Q K C L L K G K K F H H Q T C S C Y R  GCCATGTACGAACCGCCAGAAGGCTTGTGAGCCAGGATTTTCATATAGTGAAGAAG  P C T N R Q K A C E P G F S Y S E E V  TCGTTGTGTCCCTTCATATTGGCAAAGACCACAAATGAGCTAAGATTGTTACTTTTTTTT	CCAATGTGGGCCAACCGAGAATTTGATGAAAACA	ACATGCCAGTGTGTATGTAAAAGAAC
CTGCCCCAGAATCAACCCCTAAATCCTGGAAATGTGCCTGTGAATGTACAGAAA  C P R N Q P L N P G K C A C E C T E S  ACAGAAATGCTTGTTAAAAGGAAAGAAGTTCCACCACCAACATGCAGCTGTTACA  Q K C L L K G K K F H H Q T C S C Y R  GCCATGTACGACCGCCAGAAGGCTTGTGAGCCAGGATTTTCATATAGTGAAGAAG  P C T N R Q K A C E P G F S Y S E E V  TCGTTGTGTCCCTTCATATTGGCAAAGACCACAAATGAGCTAAGATTGTACTGTTTTT  TCGTTGTTGTCCCTTCATATTGGCAAAGACCACAAATGAGCTAAGATTGTACTGTTTTTTTT	C G A N R E F D E N	C Q C V C
ACAGAAATGCTTGTTAAAAGGAAAGATTCCACCACCAACATGCAGCTGTTACACCACATGCAGCTGTTACACCACATGCAGCTGTTACACCACATGCAGCTGTTACACACATGCAGCTGTTACACACATGCAACATGAGCTGTTACACATGAGCTTGTGAGCCAGGATTTTCATATAGTGAAGAAGACCACAAATGAGCTAAGATTGTACTGTTTTCATTTTCATATTTGAGCAAAATGAGCTAAGATTGTACTGTTTTCATTTTTTTT	CTGCCCCAGAAATCAACCCCTAAATCCTGGAAAAT	ATGTGCCTGTGAATGTACAGAAAGTCC
ACAGAAATGCTTGTTAAAAGGAAAGAAGTTCCACCAAACATGCAGCTGTTACACACATGCAGCATGCAGCTGTTACACACATGCAGCTGTTACACACATGCAGAACATTTTCATATAGTGAAGAAGACTTGTGAGGCTTGTGAGCCAGGATTTTCATATAGTGAAGAAGACATGTGAAGAAGACTTGTGAGAAGACCACAAATGAGCTAAGATTGTACTGTTTTCATATTGTACTGTTTTCATATTGTACTGTTTTTTTT	P R N Q P L N	A C E C T E
GCCATGTACGAACCGCCAGAAGGCTTGTGAGCCAGGATTTTCATATAGTGAAGAAGGCTTGTGAGCCAGGATTTTCATATAGTGAAGAAGGCTTGTGAGCCAGGATTTTCATATAGTGAAGAAGAAGACCAGGATTTTCATATAGTGAAGAAGACAAGAAGACCACAAATGAGATTGTACTGTTTTTTTT	ACAGAAATGCTTGTTAAAAGGAAAGAAGGTTCCACC	CACCAAACATGCAGCTGTTACAGACG
GCCATGTACGAACGCCTTGTGAGCCAGGATTTTCATATAGTGAAGAAG'++++++  P C T N R Q K A C E P G F S Y S E E V  TCGTTGTGTCCTTCATATTGGCAAAGACCACAAATGAGCTAAGATTGTACTGTTTT	K C L L K G K K F H	A C S C Y
TCGTTGTCCCTTCATATTGGCAAAGACCACAAATGAGCTAAGATTGTACTGTTTT	GCCATGTACGAACCGCCAGAAGGCTTGTGAGCCAG	GGATTTTCATATAGTGAAGAAGTGTG
TCGTTGTCCCTTCATATTGGCAAAGACCACAAATGAGCTAAGATTGTACTGTTTT	C T N R Q K A C E P	F S Y S F
+	TCGTTGTCCCTTCATATTGGCAAAGACCACAAA	ATGAGCTAAGATTGTACTGTTTTCCA

FIG. 20

MATCH WITH FIG. 2D



## MATCH WITH FIG. 2C

1141	GTTCATCGATTTTCTATTATGGAAAACTGTGTTGCCACAGTAGAACTGTCTGT
1201	GAGACCCTTGTGGGTCCATGCTAACAAGACAAAAGTCTGTCT
1261	. TAACTTTACAGAAATGGACTGGAGCTCATCTGCAAAAGGCCTCTTGTAAAGACTGGTTTT
1321	CTGCCAATGACCAAACAGCCAAGATTTTCCTCTTGTGATTTCTTTAAAAGAATGACTATA
1381	TAATTTATTTCCACTAAAATATTGTTTCTGCATTCATTTTTTTATAGCAACAACAATTGGT
1441	. AAAACTCACTGTGATCAATATTTTTTATCATGCAAAATATGTTTAAAATAAAATGAAAA
1501	TTGTATTATAAAAAAAAAA ++

FIG. 2D



1 Pdgfa .MRTLACLLL LGCGYLAHVL AEEAEIPREV IERLARSOIH SIRDLORLLE Pdgfb MNRCWA.LFL SLCCYLRLVS AEGDPIPEEL YEMLSOHSIR SFDDLORLLH VegfMNFLL SWVHWSLALL LY	Pdgfo IDSVGSEDSL DTSLRAHCVH ATKHVPEKRP LPIRRKRSIEEAVP Pdgfb GDP.GEEDGA ELDLNMTRSH SGGELESLARGRRSLG SLTIAEPAMI Vegf APMAEGGGO NHHEVVKFMD .VYQR	Pdgfa AVCKTRTVIY EIPRSQVDPT SANFLIWPPC VEVKRCTGCC NTSSVKCOPS Pdgfb AECKTRTEVF EISRRLIDRT NANFLVWPPC VEVQRCSGCC NNRNVCCRPT Vegf SYCHPIETLY DIFGEYPDEIEYIFKPSC VPLMRCGCCC NDEGLECVPT Vegf2 TCCMPREVCI DVGKEFGVATNTFFKPPC VSVYRCGCCC NSEGLCCMNI	Pdgfa RVHHRSVKVA KVEYVRKKPK LKEVQVRLEE HLEGAG AT Pdgfb QVQLRPVQVR KIEIVRKKPI FKKATVTLED HLACKG ETVAAARPVT Vegf EESNITMQIM RIK.PHQC QHIGEMSFLQ HNKCECRPKK DRARQEKKSV Vegf2 STSYLSKTLF EIT.VPLSQC PKPVTISFAN HTSGRQMSKL DVYRQVHSII
1ERLARSO1H YEMLSDHS1R	LPIRRKRSI. .LARGRRSLG .VYQR	VEVKRCTGCC VEVQRCSGCC VPLMRCGCCC VSVYRCGCCC	HLEGAG HLAGKG HNKGEGRPKK HTSGRGMSKL
AEEAE IPREV AEGOP IPEEL LY	ATKHVPEKRP SGGELES NHHEVVKFMD YNTEILKSID	SANFL IMPPC NANFL VMPPC EY I FKPSC NTFFKPPC	LKEVQVRLEE FKKATVTLED QHIGEMSFLQ PKPVTISFAN
LGCGYLAHVL SLCCYLRLVS SWVHWSLALL LYPEYWKMYK	DTSLRAHGVH ELDLNMTRSH GGGQ EETIKFAAAH	E I PRSQVDP T E I SRRL I DR T D I F QE YPDE I DVGKEFGVAT	KVEYVRKKPK KIEIVRKKPI RIK.PHOC EIT.VPLSOC
1 .MRTLACLLL MNRCWA.LFL MNFLL	51 IDSVGSEDSL GDP.GEEDGA APMAE	101 AVCKTRTV1Y AECKTRTEVF SYCHPIETLV TQCMPREVC1	151 RVHHRSVKVA QVQLRPVQVR EESNITMQIM STSYLSKTLF
Pdgfa Pdgfb Vegf Vegf	Pdgío Pdgíb Vegí Vegí	Pdgfa Pdgfb Vegf Vegf	Pdgfa Pdgfb Vegf Vegf2

**-1**G. 3A



RTVRVRRPPK CKHRKFKHTH DKTALKETLG KSRYKSWSVY VGARCCLMPW SLPCPHP NYMMNNHICR CLAQEDFMFS SDAGDDSTDG	A	DKPRR	Pdgfa
RTVRVRRPPK KSRYKSWSVY NYMMNHICR	RAGLRPASCG	DKPRR	351
	LDEETCOCVC	LELNERTCRC	SCYRRPCTNR
201 Pdgía TSLNPD YREEDTDVR. Pdgíb RSPGGSQEOR AKTPOTRVTI Vegí RGKGKGOKRKRK Vegí2 RRSLPATLPO COAANKTCPT	Pdgfa	Pdgfa	351
Pdgía Pdgíb Vegí Vegí	Pdgía Pdgíb Vegí Vegí2	Pdgfa Pdgfb Vegf Vegf2	Pdgfa Pdgfb Vegf Vegf

FIG. 3B

#### PERCENTAGE (%) OF AMINO ACID IDENTITIES BETWEEN EACH PAIR OF GENES IS SHOWN IN THE FOLLOWING TABLE

	PDGFlpha	PDGFβ	VEGF	VEGF-2
PDGF $\alpha$				
PDGFβ	48.0			
VEGF	20.7	22.7		
VEGF-2	23.5	22.4	30.0	

FIG. 4

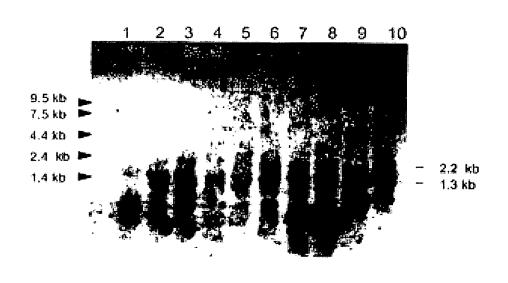


Lane 1. normal breast tissue Lane 2. breast tumor tissue Lane 3-9. breast tumor cell lines.

Expression of VEGF2 mRNA in Human Breast Tumor Cells



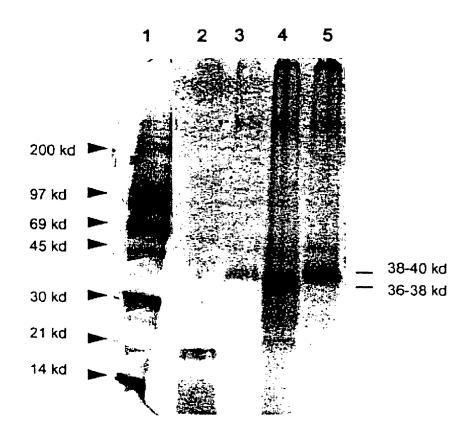
#### **Expression of VEGF-2 mRNA in Human Adult Tissues**



- 1. Ovary
- 2. Testés
- 3. Gall Blader
- 4. Kidney
- 5. Liver

- 6. Lung
- 7. Spleen
- 8. Prostate
- 9. Hippocampus
- 10. Heart





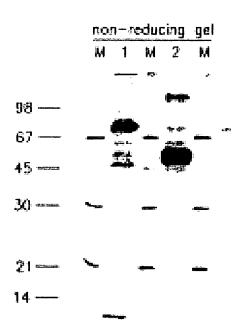
Lane 1: 14-C and rainbow M.W. marker

Lane 2: FGF control

Lane 3: VEGF2 (M13-reverse & forward primer)
Lane 4: VEGF2 (M13-reverse & VEGF-F4 primer)
Lane 5: VEGF2 (M13-reverse & VEGF-F5 primer)

**FIG.** 7



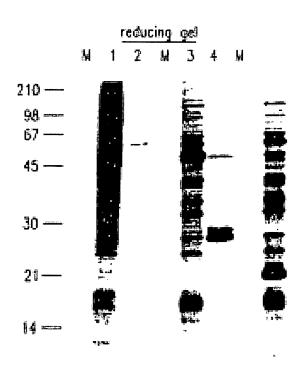


Lane M: Marker

Lane 1: Vector medium Lane 2: VEGF2 medium

FIG. 8A



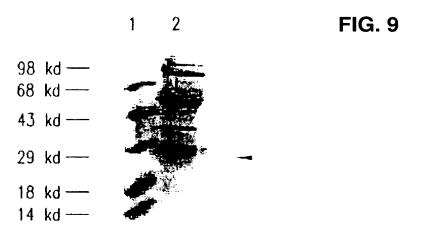


Lane M: Marker

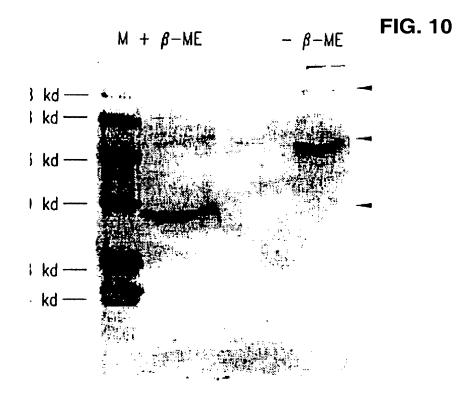
Lane 1: vector cytoplasm Lane 2: vector medium Lane 3: VEGF2 cytoplasm Lane 4: VEGF2 medium

FIG. 8B





Lane 1: Molelular weight marker Lane 2: Precipitates containing VEGF2.





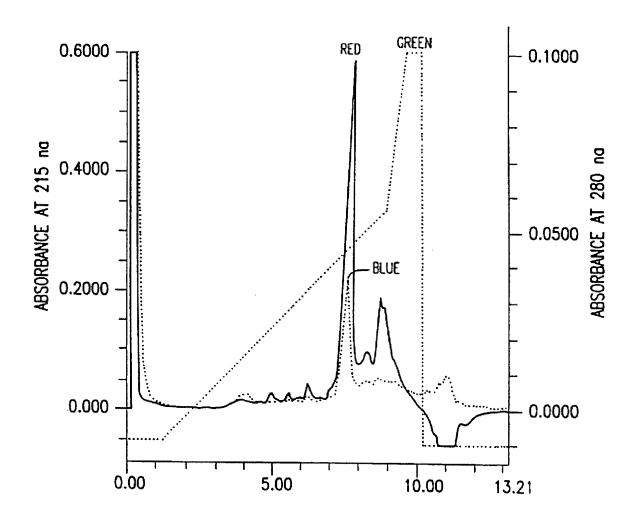


FIG. 11



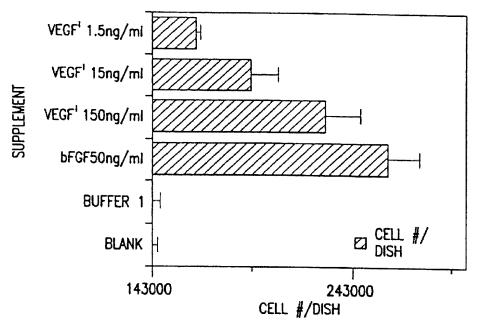


FIG. 12

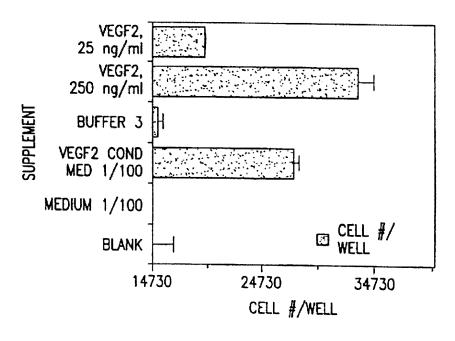


FIG. 13



tetal kidney
tetal lung
tetal lung
tetal liver
brain
tetal liver
kidney
lung
lung
lung
liver
spleen
thymus
thymus
thymus
thymus
spleen
spleen
spleen
thymus
thymus
skeletal muscl



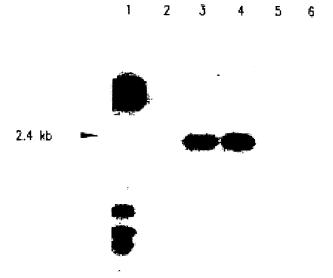
**FIG. 14A** 

M B 1 2 3 4 5 6 7 8 9 10 11 12 13



FIG. 14B

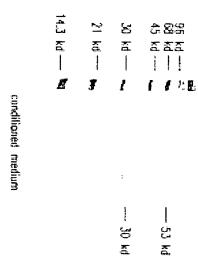




- 1.
- Molecular weight marker Umbelical vein endothelial cells 2.
- 3. Aortic smooth muscle cells
- Dermal fibroblast 4.

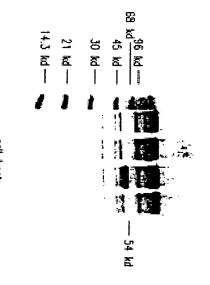
FIG. 15





- 1. Molecular weight marker
- 2. Blank
- 3. Control protein-HA
- 4. Vector control
- 5. VEGF2-HA

**FIG. 16A** 



- 1. Molecular weight marker
- 2. Blank
- 3. Control protein-HA
- 4. VEGF2-HA
- 5. Vector control

FIG. 16B



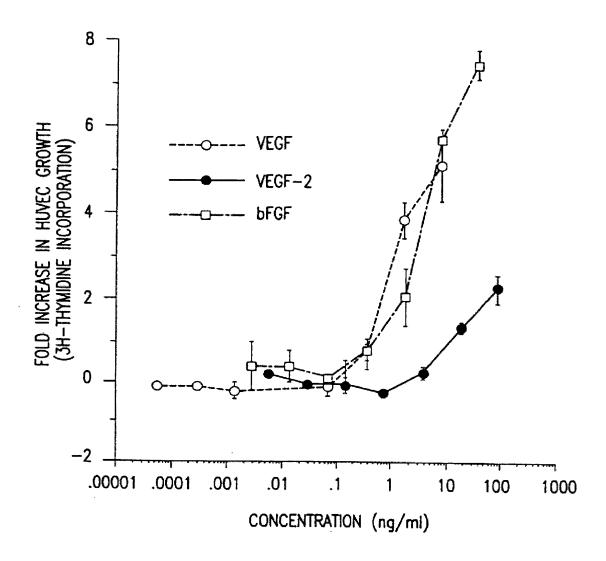


FIG. 17



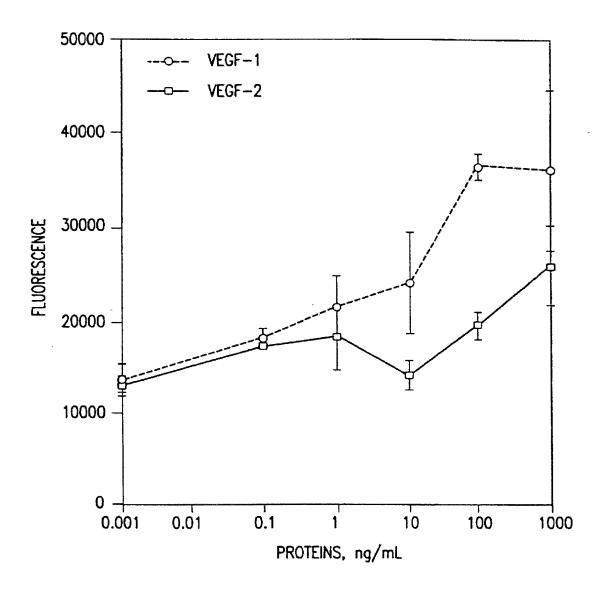


FIG. 18



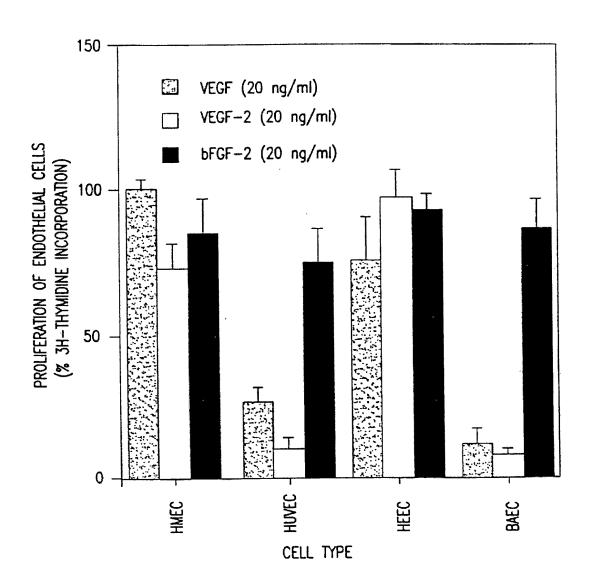


FIG. 19



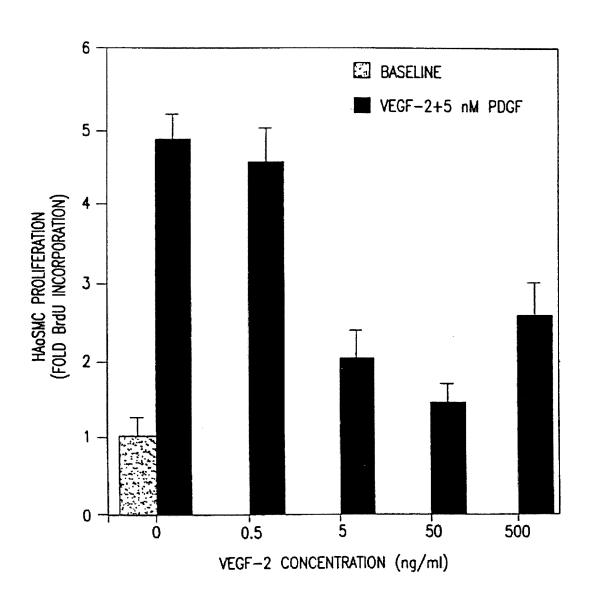


FIG. 20A

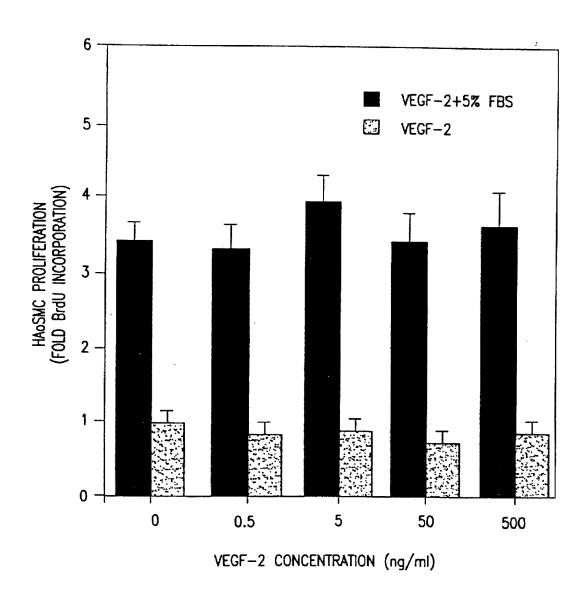


FIG. 20B



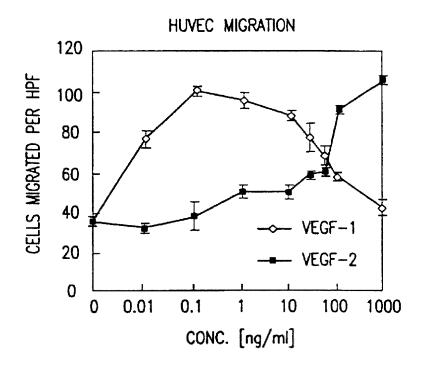


FIG. 21A

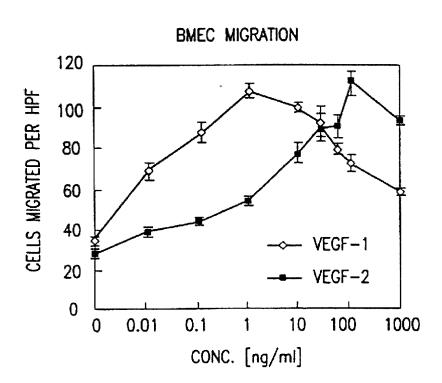


FIG. 21B

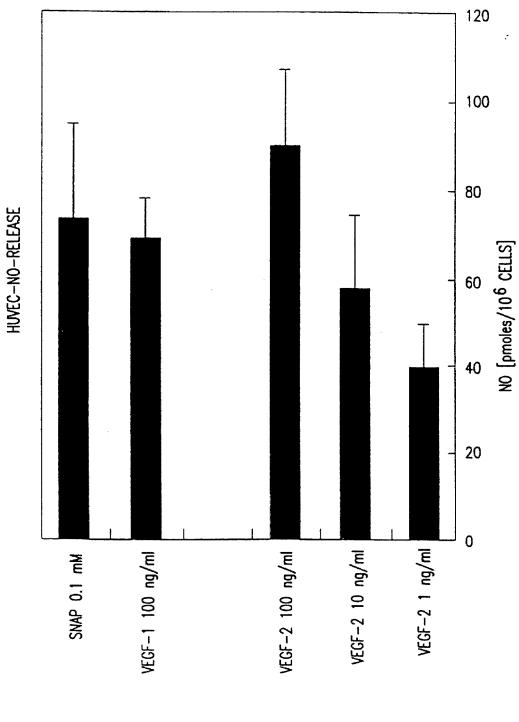


FIG. 22

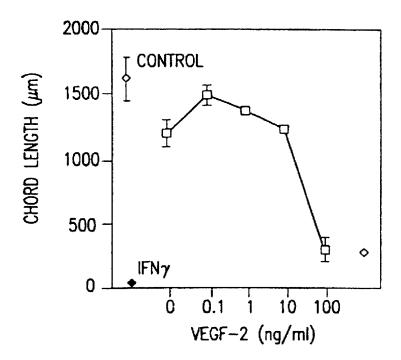


FIG. 23

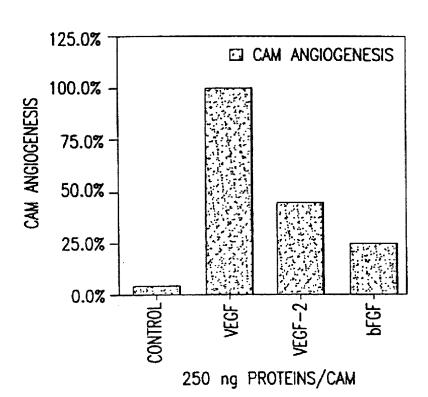
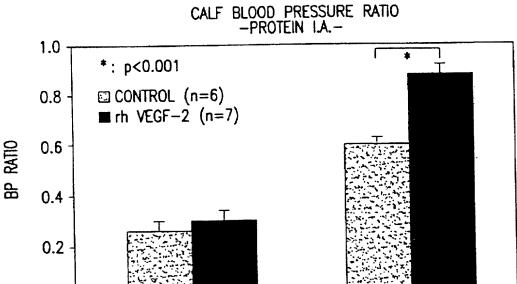


FIG. 24



0.0

32 / 68



DAY 0

**FIG. 25A** 

DAY 30

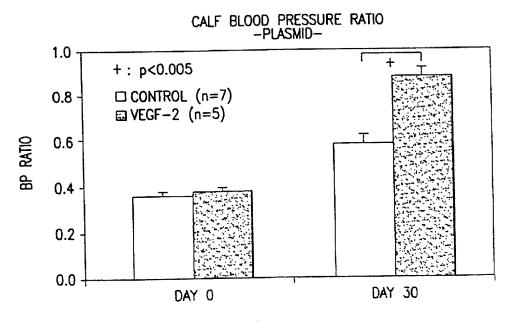
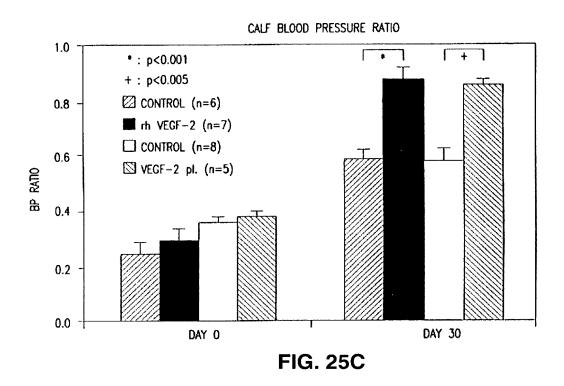
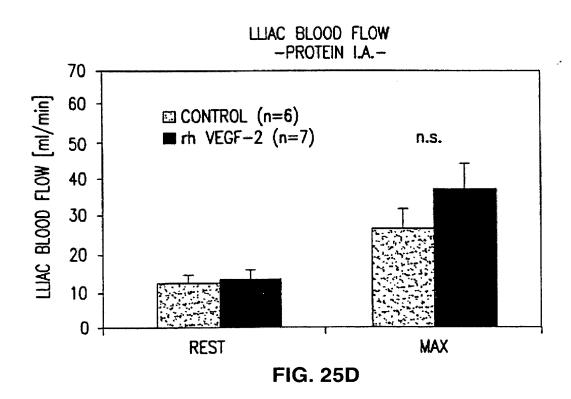


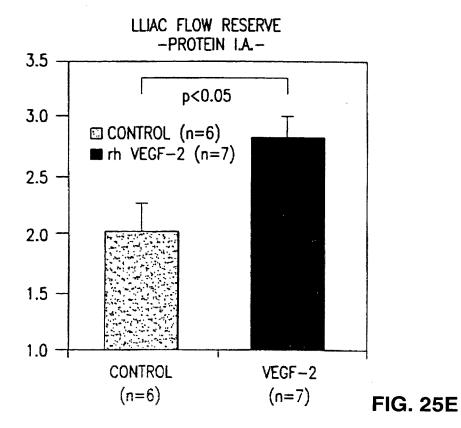
FIG. 25B







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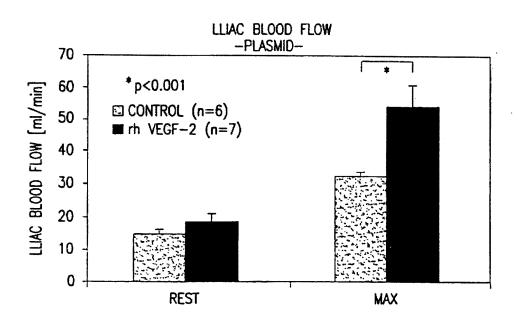


FIG. 25F



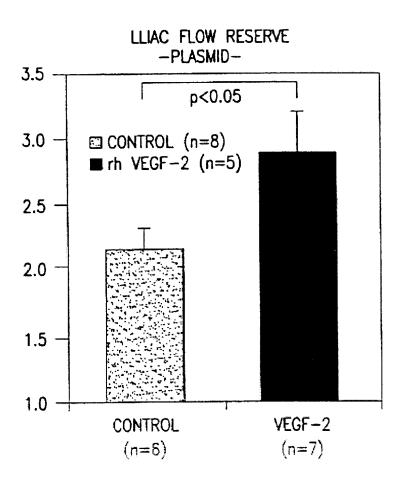


FIG. 25G



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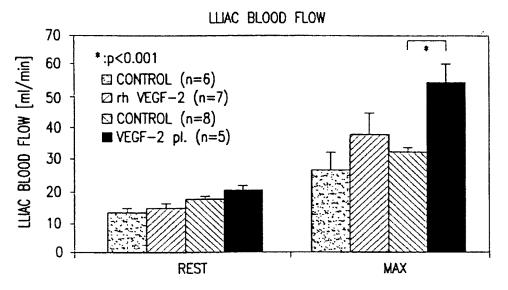


FIG. 25H

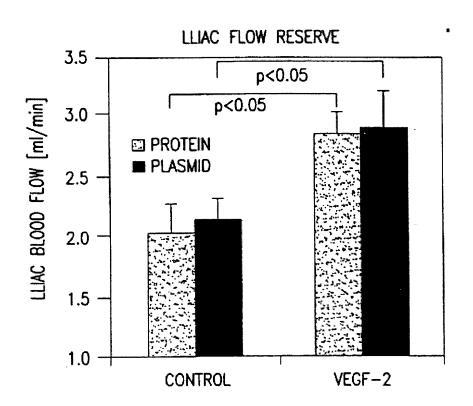


FIG. 251



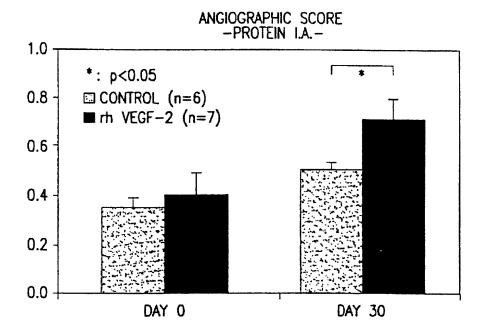


FIG. 25J

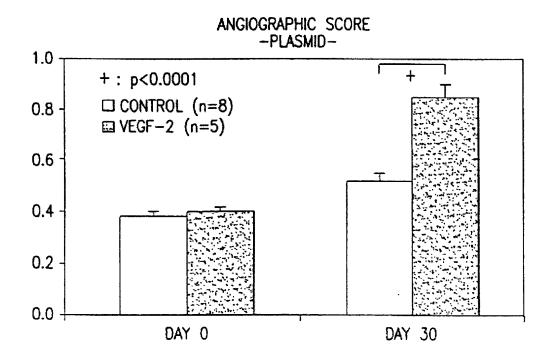


FIG. 25K



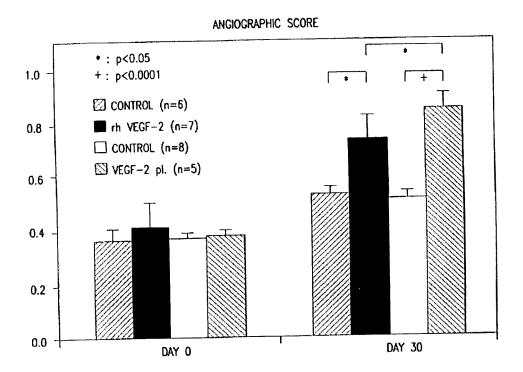


FIG. 25L

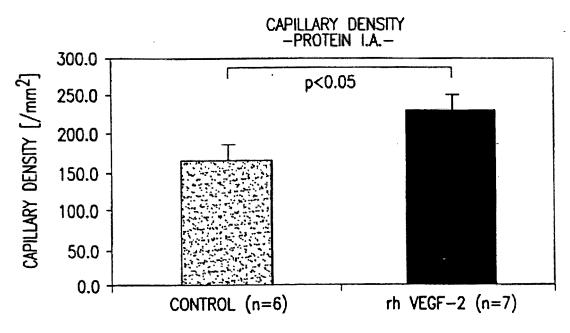
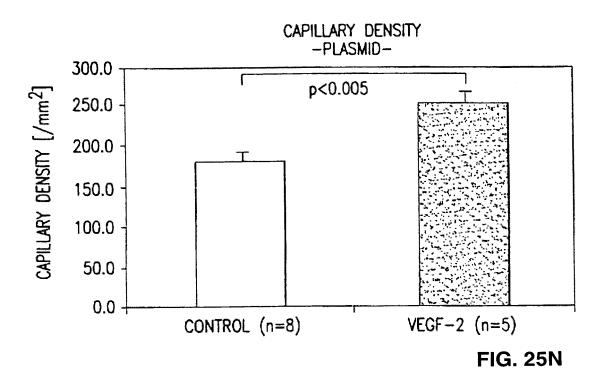
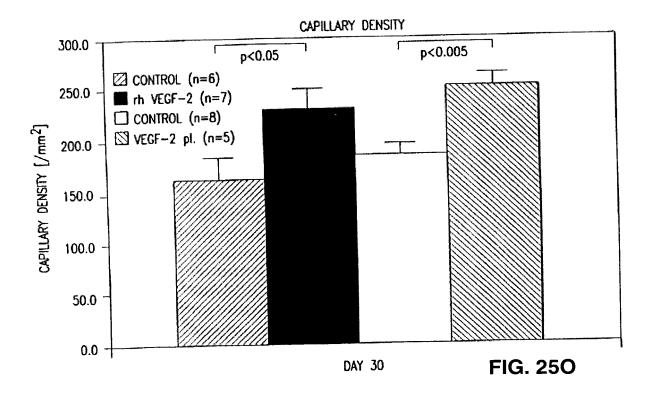


FIG. 25M









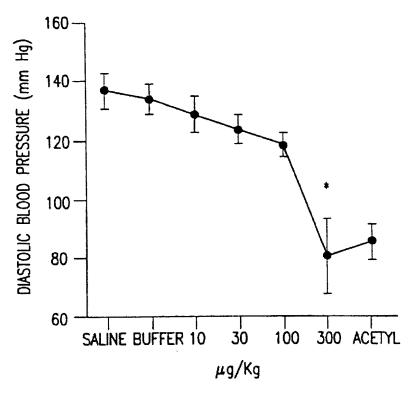


FIG. 26A

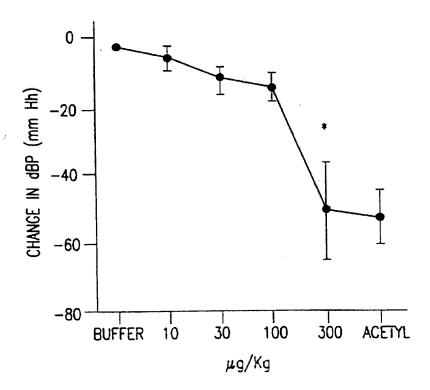


FIG. 26B



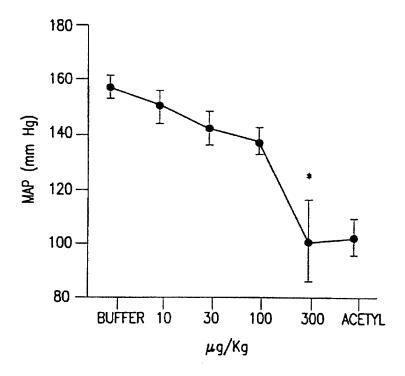


FIG. 26C

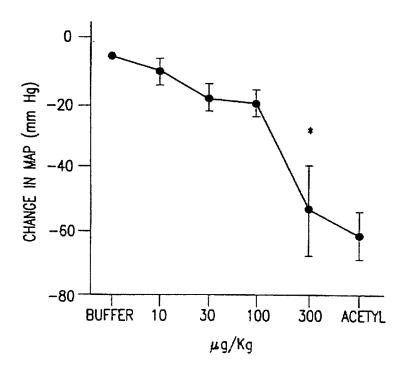
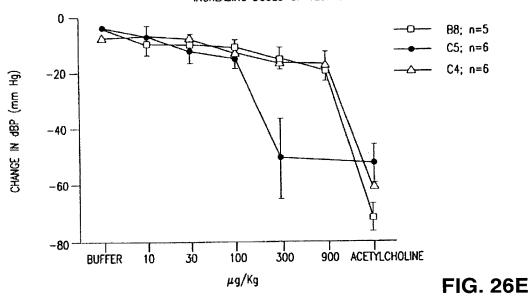


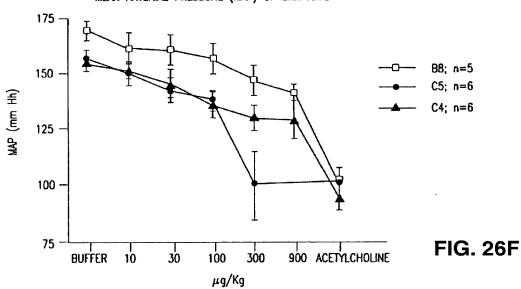
FIG. 26D



## CHANGE IN DIASTOLIC BLOOD PRESSURE OF SHR RATS GIVEN INCREASING DOSES OF VEGF-2



## THE EFFECT OF INCREASING DOSES OF VEGF-2 ON THE MEAN ARTERIAL PRESSURE (MAP) OF SHR RATS





THE EFFECT OF VEGF-2 ON THE DIASTOLIC BLOOD PRESSURE OF SHR RATS

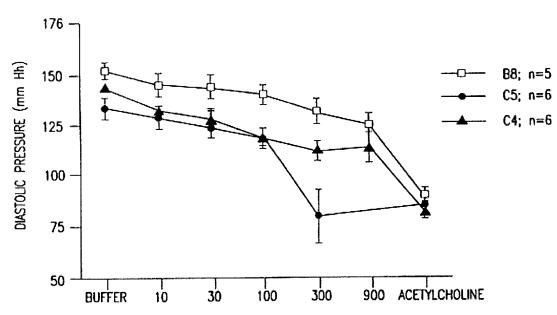


FIG. 26G



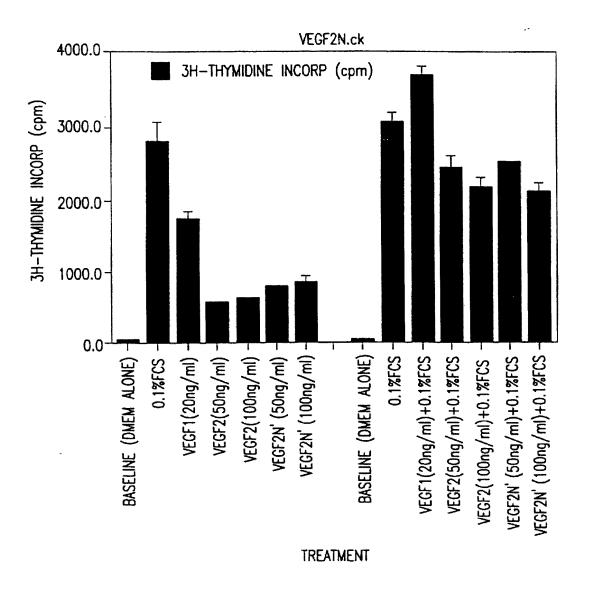


FIG. 27



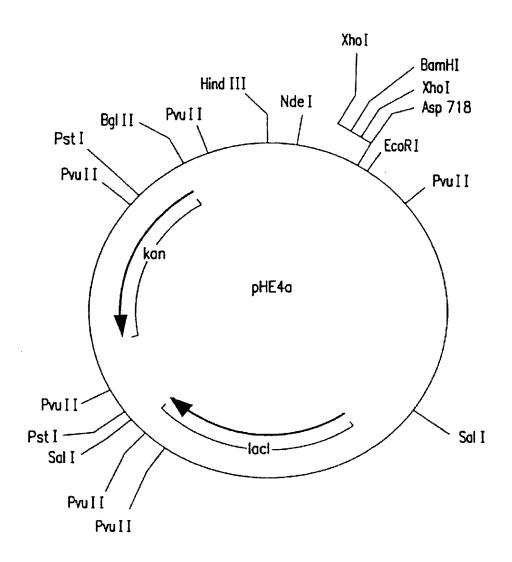


FIG. 28

AAGCITAAAAACIGCAAAAAATAG T|TIGACI OPERATOR 2

50 TAAGAT GTACCCA

94 AGAGGAGAAATTA

FIG. 29



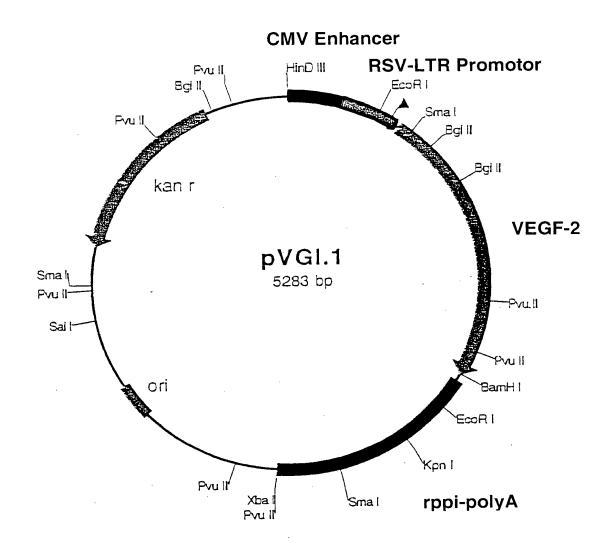


FIG. 30



Ncol
AGCTTGACCTTATGCGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG TCGAACTGGAATACGCTGAAAGGATGAACCGTCATGTAGATGCÄTAATCAGTAGCGATAATGGTACCACTACGC
CMV Enhancer
STITIGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCCACTGACGT 150 150 150 150 150 150 150 150 150 150
CMV Enhancer
CAATGGGAGTTTGTTTTGGCACCAAAATCAACGAGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCA 
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FIG.31A

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AATGGGCGGTAGGGCAACATGCTTATGTAACGGTGAGTTAGCAALATGCLITATAAGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG	0
- CMV Enhancer	
CATGCCGATTGGTGGGAGTAAGGTGGTATGATCGTGGTATGATCGTGCCTTGTTAGGAAGGCAACAGACGGGTCT 375	76
RSV-LTR Promoter	
AACACGGATTGGACGAACCACTGAATTCCGCATTGCAGAGATATTGTATTTAAGTGCCCAGCTCGATACAATAAA	2(
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FIG.31B



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	M H S L G F F L S F F	GCGAGGCGCCGCCGCCGCCGCCTTC	
RSV-LTR Promoter	Smal	TCTGTGGCGTGTTCTCTGCTCGCCGCTGCGCTGCTCCCGGGTCCTCGCGAGGCGCCCCGCCGCCGCCGCCGCCGCCGCCGCCGCC	

CICAGGCCIGAGCIGGAGAGCCIGCGCCICGGGCTGCCCCACICCGGTGCCGAAIACGIICGITICIAGACCIC \_\_ا ⋖ BgIII  $\triangleleft$ ⋖ ⋖ ⋖ ۵. ⋖ ليا  $\alpha$ Ø ⋖ ⋖ S  $\cup$ Ø > S

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FIG.31C



GAGCAGTTACGGTCTGTGTCCAGTGTAGATGACTCATGACTGTACTCTACCCAGAATATTGGAAAATGTACAAG CTCGTCAATGCCAGACACAGGTCACATCTACTTGAGTACTGACATGAGATGGGTCTTATAACCTTTTACATGTTC

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FIG.31D

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CCACGGGAGGIGIGTATAGAIGIGGGGAAGGAGITIGGAGICGCGACAACACACCTICITIAAACCICLCAIGIG		GGTGCCCTCCACATATCTACACCCCTTCCTCAAACCILAGLGLIGIIIGIGGAAAAAAAIIIGGAAGAAAAAAAAA

	1050	707	) J
PREVCIDVGKEFGVATNTFFKPPCV VEGF-2	TCCGTCTACAGATGTGGGGGTTGCTGCAATAGTGAGGGGCTGCAGTGCATGAACACCCAGCACGAGCTACCTCAGC AGGCAGATGTCTACACCCCCAACGACGTTATCACTCCCGACGTCATGTGGTCGTGGTCGTGGTCGATGGAGTCG	S V Y R C G G C C N S E G L Q C M N T S T S Y L S  VEGF-2- AAGACGITATITGAAATTACAGTGCCTCTCTCTCTCAAGGCCCCAAACCAGTAACAATCAGTTTTGCCAATCACAT	TICTGCAATAAACTTTAATGTCACGGAGAGAGAGTTCCGGGGTTTGGTCATTGTTAGTCAAAACGGTTAGTGAA

FIG.31E

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1200 TCCTGCCGATGCATGTCTAAACTGGATGTTTACAGACAAGTTCCATTCCATTATTAGACGTTCCCTGCCAGCAACA AGGACGGCTACGTACAGATTTGACCTACAAATGTCTGTTCAAGTAAGGTAATAATCTGCAAGGGACGGTCGTTGT

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CTACCACAGIGICAGGCAGCGAACAAGACCIGCCCCACCAATTACATGIGGAATAATCACATCIGCAGAIGCCTG GATGGTGTCACAGTCCGTCGCTTGTTCTGGACGGGGTGGTTAATGTACACCTTATTAGTGTAGACGTCTACGGAC

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1350 GCTCAGGAAGATITTATGTTTTCCTCGGATGCTGGAGATGACTCAACAGATGGATTCCATGACATCTGTGGACCA CGAGICCITCIAAAAIACAAAAGGAGCCIACGACCICIACIGAGIIGICIACCIAAGGIACIGIAGACACCIGGI

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FIG.31F

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TIGITCCTCGACCTACTICTCTGGACAGTCACACAGGCGTCTCGCCCCGAAGCCGGACGGTCGACACCTGGGGTG AACAAGGAGCTGGATGAAGAGACCTGTCAGTGTGTCTGCAGAGCGGGGCTTCGGCCTGCCAGCTGTGGACCCCAC Pvull Pstl

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TITCITGATCTGTCTTTGAGTACGGTCACACAGACATTITTGTTTGAGAAGGGGTCGGTTACACCCCGGTTGGCT

Z ⋖ C O S ۵. 0 ں ഗ z  $\simeq$  GAATTTGATGAAAACACATGCCAGTGTGTATGTAAAAGAACCTGCCCCAGAAATCAACCCCTAAATCCTGGAAAA CTTAAACTACTITTGTGTACGGTCACACATACATTTTCTTGGACGGGGTCTTTAGTTGGGGATTTAGGACCTTTT

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FIG.31G

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TGTGCCTGTGAATGTACAGAAAGTCCACAGAAATGCTTGTTAAAAGGAAAGAAGTTCCACCACCAAACATGCAGC ACACGGACACTTACATGTCTTTCAGGTGTCTTTACGAACAATTTTCCTTTCTTCAAGGTGGTGGTTTGTACGTCG エ エ 0 K C L L K G

ACAATGICIGCCGGTACATGCTTGGCGGTCTTCCGAACACTCGGTCCTAAAAGTATATCACTTCTTCACACAGCA TGTTACAGACGGCCATGTACGAACCGCCAGAAGGCTTGTGAGCCAGGATTTTCATATAGTGAAGAAGTGTGTCGT

0 K A C E P œ z

BamHI

ACACAGGGAAGTATAACCTTTTCTGGTGTTTACTCGATTAGATCCTAGGCATGGGACGGGTCCGAAAACAGTTTG TGTGTCCCTTCATATTGGAAAAGACCACAAATGAGCTAATCTAGGATCCGTACCCTGCCCAGGCTTTTGTCAAAC



FIG.31H



- 1875	1950	- 4 2025
AGCACCTTIGIGGTICTCACTTGGTGGAAGCTCTCTACCTGGTGTGTGGGGGAGCGTGGATTCTTCTACACACCCAA	TGTCCCGCCGCGAAGTGGAGGACCCACAAGGTAAGCTCTGCTCCTGAATTCTATCCCAAGTGCTAACTACCCTGT	TIGICITICACCCTTGAGACCTTGTAAATTGTGCCCTAGGTGTGGAGGGTCTCAGGCTAACCAGTGGGGGCACA

FIG.311

-rppi poly A

- rppi poly A —



ACCATTGTCCTACACATCCAAAACCTCCGGGTATACAGGTAAGTACTGGTCACTGAACAGAGTGTCGGTACGTTG T G G T A A C A G G A T G T T T T G G A G G C C C A T A T G T C C A T T C A T G A C C A G T G A C T T C A C A C

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- rppi poly A --

FIG.31J



TCCCTG ++++++ 2400 AGGGAC	.GGTGGCCCGG	CAACTAG
TCCTAACTGGATTGTCCTATGTGTCTTTGCTTCTGTGCTGCTCTGCCCCTGTGCTGTGCTGTGCTCTGTGACATGACCTCCCTGACATGACCTCCCTGTGACATGACGTGACATGACGTGACATGACGTGACATGACATGACATGACATGACATGACATGACATGACATGACATGACATGAATGA	GCAGTGGCACAACTGGAGGCTGGAGGCCCGGGGGCAGGTGACCTTCAGACCTTGGCACTGGAGGTGGCCCGGGCCCGGGCCCGGGCCCGGGCCCGGGCCCCGGGCCCC	CAGAAGCGCGGCATCGTGGATCAGTGCTGCACCAGCATCTGCTCTCTCT

FIG.31K



GCCCACCACTACCCTGTCCACCCCTCTGCAATGAATAAAACCTTTGAAAGAGCACTACAAGTTGTGTGTACATGC CGGGTGGTGATGGGACAGGTGGGGAGACGTTACTTATTTTGGAAACTTTCTCGTGATGTTCAACACATGTACTGTACG

-rppi poly Arppi poly A-

GCTGTCTAGACGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACATA CGACAGATCTGCATTAGTACCAGTATCGACAAAGGACACACTTTAACAATAGGCGAGTGTTAAGGTGTTGTAT Pvull Xbal

FIG.31L



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GACGGGCGAAAGGTCAGCCCTTTGGACAGCACGGTCGACGTAATTACTTAGCCGGTTGCGCGCCCCTCTCCGCCA CIGCCCGCITTCCAGICGGGAAACCIGICGIGCCAGCIGCATI'AAIGAAICGGCCAACGCGGGGGGGGGGGGGG

AACGCATAACCCGCGAGAAGGCGAGCGAGTGACTGAGCGACGCGAGCCAGCAAGCCGACGCGCTCGCCAT TCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAA AGTCGAGTGAGTTTCCGCCATTATGCCAATAGGTGTCTTAGTCCCCTATTGCGTCCTTTCTTGTACACTCGTTTT GGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAG CCGGTCGTTTTCCGGTCCTTGGCATTTTTCCGGCGCAACGACCGCAAAAAGGTATCCGAGGCGGGGGGGACTGCTC

## FIG.31M



CATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCT GTAGTGTTTTTAGCTGCGAGTTCAGTCTCCACCGCTTTGGGCTGTCCTGATATTTCTATGGTCCGCAAAGGGGGA

CCTTCGAGGGAGCACGCGAGAGACAAGGCTGGGACGGCGAATGGCCTATGGACAGGCGGAAAGAGGGGAAGCCCT GGAAGETECETTEGEGETETECTATECGACECTGECGGTTÄCEGGATACETGTECGGCTTTETECTECTTEGGGA

TCGCACCGCGAAAGAGTATCGAGTGCGACATCCATAGAGTCAAGCCACATCCAGCAAGCGAGGTTCGACCCGACA AGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGT

GIGCACGAACCCCCCGTICAGCCCCGACCGCTTGCGCTTAICCGGTAACTATCGTCITGAGTCCAACCCGGTAAGA CACGTGCTTGGGGGCCAAGTCGGGCTGGCGACGCGGAATAGGCCATTGATAGCAGAACTCAGGTTGGGCCATTCT

GTGCTGAATAGCGGTGACCGTCGTGACCATTGTCCTAATCGTCTCGCTCCATACATCCGCCACGATGTCTC

FIG.31N



AAGAACTTCACCACCGGATTGATGCCGATGTGATCTTCTTGTCATAAACCATAGACGCGAGACGATTCGGTCAA TICTIGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCAGTT

 AAGCAGCAGATTACGCGCAGAAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAG TTCGTCGTCTAATGCGCGTCTTTTTTCCTAGAGTTCTTCTAGGAAACTAGAAAGATGCCCCAGACTGCGAGTC

ACCTTGCTTTTGAGTGCAATTCCCTAAAACCAGTACTCTAATAGCAGCTGGTTTCGCCGGTAGCACGGAGGGGTG TGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCGTCGACCAAAGCGGCCATCGTGCCTCCCCAC Sall

FIG.310

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TCCTGCAGTTCGGGGGCATGCGCGGATAGCCGCTGCTGGTTTCCTGGATGCCGACGGATTTGCACTGCCGG AGGACGTCAAGCCCCCGTACCTACGCGCCTATCGGCGACGACCAAAGGACCTACGGCTGCCTAAACGTGACGGCC

TAGAACTCCGCGAGGTCGTCCAGCCTCAGGCAGCTGAACCAACTCGCGAGGGGATCGAGCCCGGGGTGGGCG ATCTIGAGGCGCTCCAGCAGGTCGGAGTCCGTCGACTTGGTTGAGCGCTCCCCTAGCTCGGGCCCCCACCCGC

TICTIGAGGICGTACTCTAGGGGCGCGACCTCCTAGTAGGTCGGCCGCAGGGCCTTTTGCTAAGGCTTCGGGTTG AAGAACTCCAGCATGAGATCCCCGCGCTGGAGGATCATCCAGCCGGCGTCCCGGAAAACGATTCCGAAGCCCAAC

FIG.31P



GGGTCTCAGGGCGAGTCTTCTTGAGCAGTTCTTCCGCTATCTTCCGCTACGCGACGCTTAGCCCTCGCCGCTATG CCCAGAGTCCCGCTCAGAAGACTCGTCAAGAAGGCGATAGAAGGCGATGCGCTGCGAATCGGGAGCGGCGATAC

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4275 GCATTICGIGCICCTICGCCAGICGGGTAAGCGGCGGTICGAGAAGICGTIATAGIGCCCCAICGGIIGCGATACA CGTAAAGCACGAGGAAGCGGTCAGCCCATTCGCCGCCAAGCTCTTCAGCAATATCACGGGTAGCCAACGCTATGT

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GGACTATCGCCAGGCGGTGTGGGTCGGCCGGTGTCAGCTACTTAGGTCTTTTCGCCGGTAAAAGGTGGTACTATA CCTGATAGCGGTCCGCCACACCCCAGCCGGCCACAGTCGATGAATCCAGAAAAGCGGCCATTTTCCACCATGATAT

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FIG.31Q

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TCGGCAAGCAGGCATCGCCATGGGTCACGACGAGGATCCTCGCCGTCGGGCATGCGCCTTGAGCCTGGCGAACA AGCCGTTCGTCCGTAGCGGTACCCAGTGCTGCTCTAGGAGCGGCAGCCCGTACGCGGGGAACTCGGACCGCTTGT

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0054 +----+ GTTCGGCTGGCGCGCGCCCTGATGCTCTTCGTCCAGATCATCCTGATCGACAAGACCGGCTTCCATCCGAGTAC CAAGCCGACCGCGCTCGGGGACTACGAGAAGCAGGTCTAGTAGGACTAGCTGTTCTGGCCGAAGGTAGGCTCATG

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CACGAGCGAGCTACGCTACAAAGCGAACCAGCTTACCCGTCCATCGGCCTAGTTCGCATACGTCGGCGGT GIGCICGCICGATGCGATGTTICGCTTGGTGGTCGAATGGGCAGGTAGCCGGATCAAGCGTATGCAGCCGCCGCA

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FIG.31R



4650 AACGTAGTCGGTACTACCTATGAAAGAGCCGTCCTCGTTCCACTCTACTGTCCTCTAGGACGGGGCCGTGAAGCG TIGCAICAGCCATGATGGATACTITCICGGCAGGAGCAAGGIGAGATGACAGGAGATCCTGCCCGGCACTICGC

 $\mathcal{C}$ لبا > م C O S S Σ Ø ⋖ CCAATAGCAGCCAGTCCCTTCCCGCTTCAGTGACAACGTCGAGCACAGCTGCGCAAGGAACGCCCGTCGTGGCCA GGTTATCGTCGGTCAGGGAAGGGCGAAGTCACTGTTGCAGCTCGTGTCGACGCGTTCCTTGCGGGCAGCACCGGT

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GGCGCCCCTGCGCTGACAGCCGGAACACGGCGGCATCAGAGCAGCCGATTGTCTGTTGTGCCAGTCATAGCCGA CCGCGGGGACGCGACTGTCGCCCTTGTGCCGCCGTAGTCTCGTCGGCTAACAGACAACACGGGTCAGTATCGGCT

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4950 TATCGGAGAGGTGGGTTCGCCGGCCTCTTGGACGCACGTTAGGTAGAACAAGTTAGTACGCTTTGCTAGGAGTAG ATAGCCTCTCCACCCAAGCGGCGGAGAACCTGCGTGCAATCCATCTTGTTCAATCATGCGAAACGATCCTCATC

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FIG.31T

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5025 GACAGAGAACTAGTCTAGAACTAGGGGACGCGGTAGTCTAGGAACCGCCGTTCTTTCGGTAGGTCAAATGAAACG CIGICICITGAICAGAICITGAICCCCIGCGCCAICAGAICCIIGGCGGCAAGAAAGCCAICCAGIITACIIIGC

Pvull

TCCCGAAGGGTTGGAATGGTCTCCCGCGGGGTCGACCGTTAAGGCCAAGCGAACGACAGGTATTTTGGCGGGTCA A G G G C T T C C C A A C C T T A C C A G G G G C C C C A G C C A T T C C G G T T C G C T T G C T A A A A A C C G C C C A G T

CTAGCTATCGCCATGTAAGCCCACTGCAAGCTACCTGCTTTCTCTTTGCGCTTGCGTTTTCCCTTGTCCAGATAG GATCGATAGCGGTACATTCGGGTGACGTTCGATGGACGAAGAGAAACGCGAACGCAAAAGGGAACAGGTCTATC

GGGTCATCGACTGTAAGTAGGCCCCAGTCGTGGCAAAGACGCCTGACCGAAAGATGCACAAGGCGAAGGAAATCG CCCAGTAGCTGACATTCATCCGGGGTCAGCACCGTTTCTGCGGACTGGCTTTCTACGTGTTCCGCTTTCTAGC

 FIG.31U